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EXAMINER

EPPS FORD, JANET L

ART UNIT	PAPER NUMBER
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1633

DATE MAILED: 01/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/713,017

Applicant(s)

CHOULIKA ET AL.

Examiner

Janet L. Epps-Ford

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 02 February 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,25 and 30-49 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 39 is/are allowed.
- 6) ☒ Claim(s) 1,25,30-38 and 40-45 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

#### ***Response to Arguments***

#### ***Claim Rejections - 35 USC § 103***

2. Claims 1, 25, 30-38, and 40-45 remain and claims 46-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gilboa et al. (WO 89/11539 A1) in view of Enquist et al. (EP300422A2), Anderson (US Patent No. 5,629,159) and Robertson et al. (US 5,225,337), for the reasons of record set forth in the prior Office Action.
3. Applicant's arguments filed 10/20/05 have been fully considered but they are not persuasive. Applicants traverse the instant rejection on the grounds that:

"[P]revious knowledge of the elements of a patent claim is not sufficient to render the claim obvious. *Abbott Laboratories v. Syntrotron Bioresearch, Inc.*, 334 F.3d 1343 (Fed. Cir. 2003). A great many permutations of nucleic acid sequence elements are available in the molecular biology literature, a great many more techniques and approaches to combine them are possible. The general structural similarities of retroelements does not render one obvious in light of another. To establish a prima facie case of obviousness, the Office must show reasons that the skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited references and combine them in the manner claimed. *In re Rouffet*, 149 F.3d 1350, 47 U.S.P.Q. 2d 1453 (Fed. Cir. 1998). The mere possibility of combining references to obtain the Applicants' invention is not sufficient to render the invention obvious. There must also be a motivation to combine the references, and the motivation must come from the references, not from the Applicants' invention. The motivation to introduce recombinase recognition sites into the LTR regions of Gilboa or to seek alternative means to express a protein with retroviral vectors would not have lead one of ordinary skill in the art to combine the teachings of these four references to invent the claimed constructs. Rather, inventive design and experimentation were necessary. A general desire to express a protein with a retroviral vector could not have provided the ordinarily skilled artisan, at the time of the invention, with the motivation to choose, among all the available possibilities, to apply the recombination technique to the retroviral vector using the Cre/loxP and FLP/FRT systems to deliver ribozymes, and thus achieve the Applicants' successful results. Particularly in the unpredictable biotech field, one of ordinary skill would not expect that a combination of four components, each described in a different reference to achieve a different end, would perform as desired. In particular, the general need to express a protein by alternative means, combined with an awareness that one may insert recombination sites into a vector would not lead one of ordinary skill to design a novel vector that permits the elimination of a large part of the proviral

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sequences which are no longer necessary, and which can be undesirable, after integration of a sequence comprising a U3, R, or U5 region into the genome of a host cell.

For the reasons cited above, the Applicants assert that the Office has not established that claims 1, 25, 30-38, and 40-45 are obvious in light of Gilboa et al., in view of Enquist et al. Anderson, and Robertson, et al. From the perspective of an ordinarily skilled artisan at the time of the invention, the combination of these four elements was neither motivated by the existing art nor reasonably expected to be successful without undue experimentation.

Contrary to Applicant's assertion that the ordinary skilled artisan at the time of the invention would not have been enabled to make the claimed compounds without undue experimentation, Applicant's arguments do not take the place of evidence. As per MPEP § 716.01(c) [R-2] "[O]bjective evidence which must be factually supported by an appropriate affidavit or declaration to be of probative value includes evidence of unexpected results, commercial success, solution of a long-felt need, ***inoperability of the prior art***, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant. See, for example, In re De Blauwe, 736 F.2d 699, 705, 222 USPQ 191, 196 (Fed. Cir. 1984) ("It is well settled that unexpected results must be established by factual evidence." "[A]ppellants have not presented any experimental data showing that prior heat-shrinkable articles split. Due to the absence of tests comparing appellant's heat shrinkable articles with those of the closest prior art, we conclude that appellant's assertions of unexpected results constitute mere argument."). See also In re Lindner,

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457 F.2d 506, 508, 173 USPQ 356, 358 (CCPA 1972); Ex parte George, 21 USPQ2d 1058 (Bd. Pat. App. & Inter. 1991).

The instant claims are drawn to a sequence of synthetic or natural retroelements, the alleged unpredictability that Applicant's are referring to is unclear, since methods of making retroviral vectors, and various molecular cloning techniques are well known in the art.

Applicants assert that there was no motivation in the art to combine the recited references, and that the Office has not made a *prima facie* case of obviousness since it has not shown "reasons that the skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited references and combine them in the manner claimed." However, contrary to Applicant's assertions, as previously stated in the prior Office Action:

As stated in the prior Office Action, it was stated that "[I]n seeking alternative means to express a protein using retroviral vectors, one of skill in the art would have combined the teachings of Guild with regards to replication deficient retroviral vectors with the teachings of Enquist et al. with regard to the utility of recombination as a means of preparing and modifying vectors of all types, including retroviral vectors, for the known and expected property of effective insertion or removal of a sequence of interest into or from the vector." The examiner recognizes that the above statement should have recited the reference "Gilboa" instead of "Guild." However, it remains that Enquist discloses the desirability of using recombination as a means of modifying retroviral vectors (page 5, lines 43-57 and page 7, lines 26-39). A viral vector is modified by the

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insertion of loxP elements (page 5, lines 1-26) and the loxP element so included is a recognition sequence for the bacteriophage P1 Cre recombinase, which is disclosed as either inserting sequences into the viral vector, and/or removing sequences from the vector (page 9, lines 1-5). The sequence of interest may encode a polypeptide. Enquist et al. does not disclose such a viral vector wherein the Cre recombinase is encoded within the vector itself. Therefore, as per MPEP § 2144, THE EXPECTATION OF SOME ADVANTAGE IS THE STRONGEST RATIONALE FOR COMBINING REFERENCES. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. In re Sernaker, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983). As stated in the prior Office Action, modification of the teachings of Gilboa et al. with Enquist et al. would be expected to confer on the vectors of Gilboa et al. "for the known and expected property of effective insertion or removal of a sequence of interest into or from the vector." Moreover, contrary to Applicant's assertions, one of ordinary skill in the art at the time of the instant invention would have been motivated to introduce recombinase recognition sites into the LTR regions of the vectors of Gilboa et al. since Gilboa et al. expressly contemplates the introduction of recognition sites for DNA or RNA binding proteins, and Enquist et al. describe the introduction of the 34 base pair recognition site (lox site) for the DNA binding protein, Cre recombinase. Furthermore, one of ordinary skill in the art at the time of the instant invention would have been motivated to further combine the

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teachings of Anderson with regard to encoding the recombinase directly on the retroviral vector, for the known and expected property disclosed by Anderson, namely for the simultaneous removal of the recombinase enzyme along with the sequence of interest. In so doing, one of skill in the art would have prepared a recombinant vector that would integrate into the genome, wherein one could then inducibly (column 8, lines 38/55) remove sequences integrated into the genome by the retroviral vector, along with the recombinase. Finally, one of ordinary skill in the art at the time of the instant invention would have been motivated to modify the retroviral vectors of Gilboa et al. to comprise wherein the nucleotide sequence of interest encodes a ribozyme sequence because Robertson et al. teaches the desirability of utilizing retroviral vectors for specific delivery of ribozymes into cells. Given the teachings of the prior art and the knowledge of one of ordinary skill in the art, it must be considered that the ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Applicants have not provided any evidence that the combination of the cited references would not render obvious the claimed invention. Thus, it remains that the invention as a whole would have been *prima facie* obvious at the time the instant invention was made.

### ***Claim Rejections - 35 USC § 112***

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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5. Claim 30 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 30 recites the limitation "28" in line 2. There is insufficient antecedent basis for this limitation in the claim since Applicants canceled claim 28.

***Allowable Subject Matter***

6. Claim 39 is allowable over the prior art of searched.

***Conclusion***

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.




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8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 9:30 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave T. Nguyen can be reached on 517-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

  
Janet L. Epps-Ford  
Primary Examiner  
Art Unit 1633

JLE